-continued

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Gln Val His His Ala Val Cys Asp Gly Phe His Val Gly Arg Met Leu
                165                 170                 175

Asn Glu Leu Gln Gln Tyr Cys Asp Glu Trp Gln Gly Gly Ala
            180                 185                 190
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What is claimed is:

**1**. A method of determining whether an enzyme is capable of ubiquitinating a test substrate, the method comprising

(a) expressing the enzyme in a bacterial cell;

(b) expressing ubiquitin in said bacterial cell, wherein said ubiquitin is attached to a first polypeptide fragment;

(c) expressing the test substrate in said bacterial cell, wherein said substrate is attached to a second polypeptide fragment, wherein said first polypeptide fragment associates with said second polypeptide fragment to generate a reporter polypeptide on ubiquitination of the test substrate; and

(d) analyzing for the presence of said reporter polypeptide in the bacterial cell, wherein a presence of said reporter polypeptide is indicative that the enzyme is capable of ubiquitinating the test substrate.

**2**. The method of claim **1**, further expressing all the enzymes of the ubiquitinating enzyme cascade of the enzyme.

**3**. The method of claim **1**, wherein said reporter polypeptide is a detectable polypeptide or a selectable polypeptide.

**4**. The method of claim **1**, wherein said enzyme is selected from the group consisting of E3 ligase, ubiquitin E1-activating enzyme and ubiquitin E2 conjugating enzyme.

**5**. The method of claim **3**, wherein said selectable polypeptide is a split antibiotic resistance polypeptide.

**6**. The method of claim **1**, wherein said first polypeptide fragment is attached to said ubiquitin via a linker and/or wherein said second polypeptide fragment is attached to said substrate via a linker.

**7**. The method of claim **3**, wherein said detectable polypeptide is an optically detectable signal.

**8**. The method of claim **1**, wherein said analyzing is effected by bimolecular complementation of an antibiotic resistance protein.

**9**. A kit comprising:

(i) a first polynucleotide which encodes a first polypeptide fragment which is operably linked to a bacterial regulatory sequence, and a cloning site, wherein a position of said cloning site is selected such that upon insertion of a sequence which encodes a test polypeptide into said cloning site, following expression in a bacterial cell, a fusion protein is generated which comprises said test polypeptide in frame with said first polypeptide fragment; and

(ii) a second polynucleotide comprising a second nucleic acid sequence encoding a second polypeptide fragment which is attached to ubiquitin, the second nucleic acid sequence being operably linked to a bacterial regulatory sequence, wherein said first polypeptide fragment associates with said second polypeptide fragment to generate a reporter polypeptide dependent on ubiquitination of said test polypeptide.

**10**. The kit of claim **9**, wherein said reporter polypeptide is a selectable polypeptide.

**11**. The kit of claim **9**, further comprising a third polynucleotide which encodes at least one ubiquitinating enzyme.

**12**. The kit of claim **9**, wherein said first polynucleotide and/or said second polynucleotide comprises a sequence which encodes at least one ubiquitinating enzyme.

**13**. The kit of claim **9**, wherein said at least one ubiquitinating enzyme comprises:

(a) ubiquitin E1-activating enzyme and ubiquitin E2-conjugating enzyme; or

(b) E3 ligase.

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